

CD-1/ICR mice, the model animal used by the National Toxicology Program and in > 20 published studies from different laboratories reporting adverse effects of BPA (reviewed by Myers et al. 2009; Richter et al. 2007). The conclusion by Doerge et al. (2010b) that “pharmacological effects observed in early postnatal rats could overpredict those possible in primates of the same age” may thus be accurate only for the NCTR CD-SD strain of rat, a strain derived from the CD-SD rat (Latendresse et al. 2009) that, in contrast to the CD-1 mouse, has not shown low-dose effects of BPA in many toxicological studies (reviewed by vom Saal and Hughes 2005). Our present findings clearly demonstrate that adult CD-1 mice and rhesus monkeys show virtually identical clearance of unconjugated BPA from serum over the 24 hr after a single oral administration, and that both the mouse and the monkey are very similar to humans in serum-conjugated BPA over the 24 hr after administration of the same dose (Figure 7). Our findings support the consensus report on BPA from a meeting held by the German Federal Environment Agency (Umweltbundesamt) (Gies et al. 2009) that rodents are appropriate models for predicting serum levels of bioactive BPA in primates.

Many claims have been made concerning the lack of relevance of rodents for predicting the consequences of BPA exposure for primates, including humans. A large number of low-dose studies reporting adverse effects of BPA in mice have involved administered doses that our findings here and elsewhere (Taylor et al. 2008) show result in internal doses of unconjugated BPA that are already far exceeded by those found in multiple biomonitoring studies in humans (reviewed by Richter et al. 2007; Vandenberg et al. 2007, 2010a). For example, based on linearity of administered and internal dose, a 20 µg/kg oral dose of BPA is predicted to lead to an average serum concentration over 24 hr of about 0.04 ng/mL BPA in adult CD-1 mice (Table 2). This 20 µg/kg/day oral dose of BPA caused adverse effects in adult mice as well as in adult rats (Alonso-Magdalena et al. 2006; Bindhumol et al. 2003; Sakaue et al. 2001; reviewed by Richter et al. 2007). Assertions that low-dose rodent studies involving both developmental and adult exposures are irrelevant for predicting the risk posed by BPA to human health are misguided. These assertions also ignore a large body of literature showing that BPA has equal potency in both rodent and human cells (Welshons et al. 2006).

## Conclusions

Many studies have attempted to portray the inability to detect unconjugated serum BPA in one experiment conducted with a limited sample size and a relatively insensitive assay (Völkel et al. 2002) as an indication that all

administered BPA is completely metabolized during its first pass through the liver. Our findings with rhesus monkeys in the present study do not support this conclusion and indicate that the adult rhesus monkey is a valid model for predicting the serum levels of conjugated BPA after oral exposure in humans. Our findings also suggest that the mouse is a valid predictor of serum-conjugated BPA after oral exposure in humans. Finally, when the data on BPA metabolism in infant and adult rhesus monkeys reported in an FDA study (Doerge et al. 2010b) are compared with our findings in neonatal CD-1 mice (Taylor et al. 2008) and our data presented here, virtually identical age-related changes in the rate of metabolism of unconjugated BPA are evident in rhesus monkeys and CD-1 mice. These findings lead to the conclusion that the CD-1 mouse is a valid predictor of age-related changes in the rate of metabolism of BPA in rhesus monkeys and thus also likely in humans. Finally, ingestion of the currently estimated exposure level of BPA from food and beverages in the United States (0.16 µg/kg/day) is not consistent with our finding here of an average serum-unconjugated BPA concentration of about 0.5 ng/mL in rhesus monkeys and mice during the 24 hr after ingestion of 400 µg/kg/day BPA.

## CORRECTION

In the manuscript originally published online, Pierre-Louis Toutain and Céline M. Laffont were omitted from the list of authors; there were calculation errors in Tables 1–3; and the  $y$ -axis for unconjugated BPA in Figure 5 was incorrect. All of these have been corrected here.

In Supplemental Material, Part 2 (doi:10.1289/ehp.1002514), the authors have included the original data as mean, SE, and number of animals per treatment group, as well as analysis of the data from these experiments using WinNonlin (Pharsight Corporation, Cary, NC, USA) and NONMEM (ICON Development Solutions, Ellicott City, MD, USA) software that is used by the Food and Drug Administration for analyzing pharmacokinetic data.

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